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WHAT IS CLAIMED IS:

- 1 1. A method of controlling cancer suppression in a mammal having a
2 cancer suppressing gene, comprising the steps of:
3 making a substantially duplicated genetic material corresponding to the
4 genetic material of said gene, the substantially duplicated material selected from the group
5 consisting of a cloned cancer suppressing gene, a modified or defective cancer suppressing
6 gene, homologues thereof, fragments thereof, and mixtures thereof; and
7 interchanging said duplicated genetic material and the cancer suppressing gene
8 of the mammal.
- 1 2. A method of claim 1, wherein before said making a substantially
2 duplicated genetic material, determining the chromosomal location of said cancer suppressing
3 gene of the mammal.
- 1 3. A method of claim 1, wherein after said making a substantially
2 duplicated genetic material, detecting the presence or absence of an inactive cancer
3 suppressing gene of a tissue sample of the mammal to determine whether or not the tissue
4 sample cancer suppressing gene is defective or absent.
- 1 4. A method of claim 3, wherein in response to a determination that the
2 tissue sample cancer suppressing gene is either defective or absent, replacing a cancer
3 suppressing gene of the mammal with its clone.
- 1 5. A method of claim 3, wherein the determination of whether or not the
2 tissue sample cancer suppressing gene is defective or absent is accomplished by measuring
3 the amount of protein product of said cancer suppressing gene, of the tissue sample, bound by
4 an antibody specific for said protein.
- 1 6. A method of claim 5, wherein the determination of whether or not the
2 tissue sample cancer suppressing gene is defective or absent is accomplished by:
 - 3 (a) labeling said tissue sample with radioactive isotope;
 - 4 (b) lysing the labeled tissue;
 - 5 (c) reacting the protein product of said cancer suppressing gene with an
6 antibody specific for said protein thereby forming a protein/antibody immunocomplex;
 - 7 (d) autoradiographing the immunocomplex obtained in step (c); and

8 (e) determining the presence or absence of the protein product by
9 comparing the autoradiogram of step (d) with the autoradiogram of the standard protein
10 product.

1 7. The method of claim 5, wherein the determination of whether or not
2 the tissue sample cancer suppressing gene is defective or absent is accomplished by enzyme
3 immunoassay techniques.

1 8. The method of claim 5, wherein the determination of whether or not
2 the tissue sample cancer suppressing gene is defective or absent is accomplished by
3 immunocytochemistry methods.

1 9. The method of claim 5, wherein the cancer suppressing gene is the RB
2 gene and the protein product is ppRB¹¹⁰.

1 10. The method of claim 1, wherein said cancer suppressing gene is
2 replaced with substantially duplicated material selected from the group consisting of said
3 cloned cancer suppressing gene, homologues thereof, fragments thereof, and mixtures
4 thereof, for therapeutic purposes.

1 11. The method of claim 1, wherein said cancer suppressing gene is
2 replaced with substantially duplicated material selected from the group consisting of said
3 defective cancer suppressing gene, homologues thereof, fragments thereof, and mixtures
4 thereof, for facilitating the testing of the carcinogenicity of environmental influences.

1 12. The method of claim 2, wherein the location of said cancer suppressing
2 gene is determined by chromosome walking.

1 13. The method of claim 2, wherein the location of said cancer suppressing
2 gene is determined through organic markers.

1 14. A method of claim 2, wherein:
2 said chromosomal location of said cancer suppressing gene is determined by
3 testing genes of a chromosome for phenotypic expression;
4 determining one of the genes of said chromosome to be a marker gene; and
5 using chromosomal walking techniques to locate a cancer suppressing gene.

1 15. An animal genetically altered so as to have the allele of at least one
2 cancer suppressing gene selected from the group consisting of a defective allele, a homologue
3 thereof, a fragment thereof, and a mixture thereof.

1 16. An animal of claim 15, wherein said defective allele is selected from
2 the group consisting of defective alleles of RB genes, breast cancer suppressing genes,
3 Wilm's tumor suppressing genes, Beckwith-Wiedemann syndrome suppressing genes,
4 bladder transitional cell carcinoma suppressing genes, neuroblastoma suppressing genes,
5 small cell lung carcinoma suppressing genes, renal cell carcinoma suppressing genes,
6 acoustic neuroma suppressing genes, colorectal carcinoma suppressing genes, homologues
7 thereof, fragments thereof, and mixtures thereof.

1 17. An animal of claim 15, wherein said allele contains a DNA fragment
2 having at least one defective nucleotide sequence.

1 18. An animal of claim 15, wherein said defective allele contains a DNA
2 fragment having at least one defective RB nucleotide sequence.

1 19. The animal of claim 15, wherein said animal is a mouse.

1 20. A method for determining the carcinogenicity of suspected
2 environmental influences, using the animal of claim 14, comprising the steps of:
3 exposing said animal to a suspected environmental influence;
4 observing the animal for the phenotypic expression of cancer; and
5 determining carcinogenicity of the suspected environmental influence in
6 response to observing a phenotypic expression of cancer in the animal.

1 21. A method of claim 20, wherein said exposing includes exposing to a
2 source of radiation.

1 22. A method of claim 20, wherein said exposing includes exposing to
2 tobacco combustion products.

1 23. A method of claim 20, wherein said exposing includes exposing to
2 food additives.

1 24. A method of claim 20, wherein said exposing includes exposing to
2 artificial substances.

1 25. A method of claim 20, wherein said observing includes examining the
2 animal for tumor development.

1 26. A method of claim 25, wherein in response to the formation of a tumor
2 in the animal, analyzing the tumor for the presence of cancer cells.

1 27. A method of making the animal of claim 15, comprising:
2 using at least one allele of an animal cancer suppressing gene selected from
3 the group consisting of a defective allele, a homologue thereof, a fragment thereof, and a
4 mixture thereof;

5 mutating at least one animal cell with said allele to form a mutated cell;
6 introducing said mutated cell into an animal blastocyst;
7 permitting growth of the blastocyst for a given period of time sufficient to
8 incorporate said allele into its cells; repressing genetic recombinations within said cells;
9 transferring the blastocyst containing said allele into the uterus of a pseudo pregnant animal
10 for giving birth subsequently to an animal bearing said allele;
11 breeding said animal to reproduce additional animals; and
12 selecting the animal of claim 14 from said additional animals by determining
13 the presence therein of the said allele.

1 28. A method of claim 27, wherein before introducing said allele,
2 removing said blastocyst from a super ovulated animal, and wherein said blastocyst is
3 comprised of undifferentiated cells.

1 29. A method of claim 27, wherein said introducing is performed in vitro.

1 30. A pharmaceutical composition wherein the active ingredient is selected
2 from the group consisting of a naturally occurring intact cancer suppressing gene, a cloned
3 intact cancer suppressing gene, fragments thereof, homologues thereof and mixtures thereof.

1 31. A pharmaceutical composition of claim 30, wherein said naturally
2 occurring and cloned cancer suppressing gene is selected from the group consisting of RB
3 genes, breast cancer suppressing genes, Wilm's tumor suppressing genes, Beckwith-

4 Wiedemann syndrome suppressing genes, bladder transitional cell carcinoma suppressing
5 genes, neuroblastoma suppressing genes, small cell lung carcinoma suppressing genes, renal
6 cell carcinoma suppressing genes, acoustic neuroma suppressing genes, colorectal carcinoma
7 suppressing genes, homologues thereof, fragments thereof, and mixtures thereof.

1 32. A pharmaceutical composition of claim 30, wherein the active
2 ingredient is selected from the group consisting of RB cDNA, modified RB cDNA fragment,
3 clones thereof, homologues thereof and mixtures thereof.

1 33. A pharmaceutical composition of claim 31, wherein the active
2 ingredient for each of said gene is selected from the group consisting od cDNA of said gene,
3 fragments of said cDNA, homologues thereof and mixtures thereof.

1 34. A pharmaceutical composition of claim 32, wherein the cancer
2 suppressing gene is isolated from human chromosome 13 region 13q14.

1 35. A pharmaceutical composition of claim 31, wherein the cancer
2 suppressing gene and its clone each has the following nucleotide sequence:

```

5      TTCCGGTTTT TCTCAGGGGA CGTTGAAATT ATTTTTGTAA CGGGAGTCGG GAGAGGACGG      60
6      GGCGTGCCTCC CGGTGCGCGC GCGTCGTCCCT CCCCGGCGCT CCTCCACAGC TCGCTGGCTC      120
7      CCGCCGCGGA AAGGCCTC ATG CCG CCC AAA ACC CCC CGA AAA ACG GCC GCC      171
8          Met Pro Pro Lys Thr Pro Arg Lys Thr Ala Ala
9          1           5           10
10
11
12      ACC GCC GCC GCT GCC GCG GAA CCC CCG GCA CCG CCG CCG CCG CCC      219
13      Thr Ala Ala Ala Ala Ala Glu Pro Pro Ala Pro Pro Pro Pro Pro
14          15           20           25
15
16
17      CCT CCG TAG GAG GAC CCA GAG CAG GAC AGC GGC CCG GAG GAC CTG CCT      267
18      Pro Pro Glu Glu Asp Pro Glu Gln Asp Ser Gly Pro Glu Asp Leu Pro
19          30           35           40
20
21      CTC GTC AGG CTT GAG TTT GAA GAA ACA GAA GAA CCT GAT TTT ACT GCA      315
22      Leu Val Arg Leu Glu Phe Glu Glu Thr Glu Glu Pro Asp Phe Thr Ala
23          45           50           55
24
25      TTA TGT CAG AAA TTA AAG ATA CCA GAT CAT GTC AGA GAG AGA GCT TGG      363
26      Leu Cys Gln Lys Leu Lys Ile Pro Asp His Val Arg Glu Arg Ala Trp
27          60           65           70           75
28
29      TTA ACT TGG GAG AAA GTT TCA TCT GTG GAT GGA GTA TTG GGA GGT TAT      411
30      Leu Thr Trp Glu Lys Val Ser Ser Val Asp Gly Val Leu Gly Gly Tyr
31          80           85           90
32

```

33 ATT CAA AAG AAA AAG GAA CTG TGG GGA ATC TGT ATC TTT ATT GCA GCA 459
 34 Ile Gln Lys Lys Glu Leu Trp Gly Ile Cys Ile Phe Ile Ala Ala
 35 95 100 105
 36
 37 GTT GAC CTA GAT GAG ATG TCG TTC ACT TTT ACT GAG CTA CAG AAA AAC 507
 38 Val Asp Leu Asp Glu Met Ser Phe Thr Phe Thr Glu Leu Gln Lys Asn
 39 110 115 120
 40
 41 ATA GAA ATC AGT GTC CAT AAA TTC TTT AAC TTA CTA AAA GAA ATT GAT 555
 42 Ile Glu Ile Ser Val His Lys Phe Phe Asn Leu Leu Lys Glu Ile Asp
 43 125 130 135
 44
 45 ACC AGT ACC AAA GTT GAT AAT GCT ATG TCA AGA CTG TTG AAG AAC TAT 603
 46 Thr Ser Thr Lys Val Asp Asn Ala Met Ser Arg Leu Leu Lys Lys Tyr
 47 140 145 150 155
 48
 49 GAT GTA TTG TTT GCA CTC TTC AGC AAA TTG GAA AGG ACA TGT GAA CTT 651
 50 Asp Val Leu Phe Ala Leu Phe Ser Lys Leu Glu Arg Thr Cys Glu Leu
 51 160 165 170
 52
 53 ATA TAT TTG ACA CAA CCC AGC AGT TCG ATA TCT ACT GAA ATA AAT TCT 699
 54 Ile Tyr Leu Thr Gln Pro Ser Ser Ser Ile Ser Thr Glu Ile Asn Ser
 55 175 180 185
 56
 57 GCA TTG GTG CTA AAA GTT TCT TGG ATC ACA TTT TTA TTA GCT AAA GGG 747
 58 Ala Leu Val Leu Lys Val Ser Trp Ile Thr Phe Leu Leu Ala Lys Gly
 59 190 195 200
 60
 61 GAA GTA TTA CAA ATG GAA GAT GAT CTG GTG ATT TCA TTT CAG TTA ATG 795
 62 Glu Val Leu Gln Met Glu Asp Asp Leu Val Ile Ser Phe Gln Leu Met
 63 205 210 215
 64 CTA TGT GTC CTT GAC TAT TTT ATT AAA CTC TCA CCT CCC ATG TTG CTC 843
 65 Leu Cys Val Leu Asp Tyr Phe Ile Lys Leu Ser Pro Pro Met Leu Leu
 66 220 225 230 235
 67
 68 AAA GAA CCA TAT AAA ACA GCT GTT ATA CCC ATT AAT GGT TCA CCT CGA 891
 69 Lys Glu Pro Tyr Lys Thr Ala Val Ile Pro Ile Asn Gly Ser Pro Arg
 70 240 245 250
 71
 72 ACA CCC AGG CGA GGT CAG AAC AGG AGT GCA CGG ATA GCA AAA CAA CTA 939
 73 Thr Pro Arg Arg Gly Gln Asn Arg Ser Ala Arg Ile Ala Lys Gln Leu
 74 255 260 265
 75
 76 GAA AAT GAT ACA AGA ATT ATT GAA GTT CTC TGT AAA GAA CAT GAA TGT 987
 77 Glu Asn Asp Thr Arg Ile Ile Glu Val Leu Cys Lys Glu His Glu Cys
 78 270 275 280
 79
 80 AAT ATA GAT GAG GTG AAA AAT GTT TAT TTC AAA AAT TTT ATA CCT TTT 1035
 81 Asn Ile Asp Glu Val Lys Asn Val Tyr Phe Lys Asn Phe Ile Pro Phe
 82 285 290 295
 83
 84 ATG AAT TCT CTT GGA CTT GTA ACA TCT AAT GGA CTT CCA GAG GTT GAA 1083
 85 Met Asn Ser Leu Gly Leu Val Thr Ser Asn Gly Leu Pro Glu Val Glu
 86 300 305 310 315
 87
 88 AAT CTT TCT AAA CGA TAC GAA ATT TAT CTT AAA AAT AAA GAT CTA 1131
 89 Asn Leu Ser Lys Arg Tyr Glu Glu Ile Tyr Leu Lys Asn Lys Asp Leu
 90 320 325 330
 91
 92 GAT GCA AGA TTA TTT TTG GAT CAT GAT AAA ACT CTT CAG ACT GAT TCT 1179
 93 Asp Ala Arg Leu Phe Leu Asp His Asp Lys Thr Leu Gln Thr Asp Ser

94	335	340	345	
95				
96	ATA GAC AGT TTT GAA ACA CAG AGA ACA CCA CGA AAA AGT AAC CTT GAT			1227
97	Ile Asp Ser Phe Glu Thr Gln Arg Thr Pro Arg Lys Ser Asn Leu Asp			
98	350	355	360	
99				
100	GAA GAG GTG AAT GTA ATT CCT CCA CAC ACT CCA GTT AGG ACT GTT ATG			1275
101	Glu Glu Val Asn Val Ile Pro Pro His Thr Pro Val Arg Thr Val Met			
102	365	370	375	
103				
104	AAC ACT ATC CAA CAA TTA ATG ATG ATT TTA AAT TCA GCA AGT GAT CAA			1323
105	Asn Thr Ile Gln Gln Leu Met Met Ile Leu Asn Ser Ala Ser Asp Gln			
106	380	385	390	395
107				
108	CCT TCA GAA AAT CTG ATT TCC TAT TTT AAC AAC TGC ACA GTG AAT CCA			1371
109	Pro Ser Glu Asn Leu Ile Ser Tyr Phe Asn Asn Cys Thr Val Asn Pro			
110	400	405	410	
111				
112	AAA GAA AGT ATA CTG AAA AGA GTG AAG GAT ATA GGA TAC ATC TTT AAA			1419
113	Lys Glu Ser Ile Leu Lys Arg Val Lys Asp Ile Gly Tyr Ile Phe Lys			
114	415	420	425	
115				
116	GAG AAA TTT GCT AAA GCT GTG GGA CAG GGT TGT GTC GAA ATT GGA TCA			1467
117	Glu Lys Phe Ala Lys Ala Val Gly Gln Gly Cys Val Glu Ile Gly Ser			
118	430	435	440	
119				
120	CAG CGA TAC AAA CTT GGA GTT CGC TTG TAT TAC CGA GTA ATG GAA TCC			1515
121	Gln Arg Tyr Lys Leu Gly Val Arg Leu Tyr Tyr Arg Val Met Glu Ser			
122	445	450	455	
123				
124	ATG CTT AAA TCA GAA GAA CGA TTA TCC ATT CAA AAT TTT AGC AAA			1563
125	Met Leu Lys Ser Glu Glu Arg Leu Ser Ile Gln Asn Phe Ser Lys			
126	460	465	470	475
127				
128	CTT CTG AAT GAC AAC ATT TTT CAT ATG TCT TTA TTG GCG TGC GCT CTT			1611
129	Leu Leu Asn Asp Asn Ile Phe His Met Ser Leu Leu Ala Cys Ala Leu			
130	480	485	490	
131				
132	GAG GTT GTA ATG GCC ACA TAT AGC AGA AGT ACA TCT CAG AAT CTT GAT			1659
133	Glu Val Val Met Ala Thr Tyr Ser Arg Ser Thr Ser Gln Asn Leu Asp			
134	495	500	505	
135				
136	TCT GGA ACA GAT TTG TCT TTC CCA TGG ATT CTG AAT GTG CTT AAT TTA			1707
137	Ser Gly Thr Asp Leu Ser Phe Pro Trp Ile Leu Asn Val Leu Asn Leu			
138	510	515	520	
139				
140	AAA GCC TTT GAT TTT TAC AAA GTG ATC GAA AGT TTT ATC AAA GCA GAA			1755
141	Lys Ala Phe Asp Phe Tyr Lys Val Ile Glu Ser Phe Ile Lys Ala Glu			
142	525	530	535	
143				
144	GGC AAC TTG ACA AGA GAA ATG ATA AAA CAT TTA GAA CGA TGT GAA CAT			1803
145	Gly Asn Leu Thr Arg Glu Met Ile Lys His Leu Glu Arg Cys Glu His			
146	540	545	550	555
147				
148	CGA ATC ATG GAA TCC CTT GCA TGG CTC TCA GAT TCA CCT TTA TTT GAT			1851
149	Arg Ile Met Glu Ser Leu Ala Trp Leu Ser Asp Ser Pro Leu Phe Asp			
150	560	565	570	
151				
152	CTT ATT AAA CAA TCA AAG GAC CGA GAA GGA CCA ACT GAT CAC CTT GAA			1899
153	Leu Ile Lys Gln Ser Lys Asp Arg Glu Gly Pro Thr Asp His Leu Glu			
154	575	580	585	

155
 156 TCT GCT TGT CCT CTT AAT CTT CCT CTC CAG AAT AAT CAC ACT GCA GCA 1947
 157 Ser Ala Cys Pro Leu Asn Leu Pro Leu Gln Asn Asn His Thr Ala Ala
 158 590 595 600
 159
 160 GAT ATG TAT CTT TCT CCT GTA AGA TCT CCA AAG AAA AAA GGT TCA ACT 1995
 161 Asp Met Tyr Leu Ser Pro Val Arg Ser Pro Lys Lys Lys Gly Ser Thr
 162 605 610 615
 163
 164 ACG CGT GTA AAT TCT ACT GCA AAT GCA GAG ACA CAA GCA ACC TCA GCC 2043
 165 Thr Arg Val Asn Ser Thr Ala Asn Ala Glu Thr Gln Ala Thr Ser Ala
 166 620 625 630 635
 167
 168 TTC CAG ACC CAG AAG CCA TTG AAA TCT ACC TCT CTT TCA CTG TTT TAT 2091
 169 Phe Gln Thr Gln Lys Pro Leu Lys Ser Thr Ser Leu Ser Leu Phe Tyr
 170 640 645 650
 171
 172 AAA AAA GTG TAT CGG CTA GCC TAT CTC CGG CTA AAT ACA CTT TGT GAA 2139
 173 Lys Lys Val Tyr Arg Leu Ala Tyr Leu Arg Leu Asn Thr Leu Cys Glu
 174 655 660 665
 175
 176 CGC CTT CTG TCT GAG CAC CCA GAA TTA GAA CAT ATC ATC TGG ACC CTT 2187
 177 Arg Leu Leu Ser Glu His Pro Glu Leu Glu His Ile Ile Trp Thr Leu
 178 670 675 680
 179
 180 TTC CAG CAC ACC CTG CAG AAT GAG TAT GAA CTC ATG AGA GAC AGG CAT 2235
 181 Phe Gln His Thr Leu Gln Asn Glu Tyr Glu Leu Met Arg Asp Arg His
 182 685 690 695
 183
 184 TTG GAC CAA ATT ATG ATG TGT TCC ATG TAT GGC ATA TGC AAA GTG AAG 2283
 185 Leu Asp Gln Ile Met Met Cys Ser Met Tyr Gly Ile Cys Lys Val Lys
 186 700 705 710 715
 187
 188 AAT ATA GAC CTT AAA TTC AAA ATC ATT GTA ACA GCA TAC AAG GAT CTT 2331
 189 Asn Ile Asp Leu Lys Phe Lys Ile Ile Val Thr Ala Tyr Lys Asp Leu
 190 720 725 730
 191
 192 CCT CAT GCT GTT CAG GAG ACA TTC AAA CGT GTT TTG ATC AAA GAA GAG 2379
 193 Pro His Ala Val Gln Glu Thr Phe Lys Arg Val Leu Ile Lys Glu Glu
 194 735 740 745
 195
 196 GAG TAT GAT TCT ATT ATA GTA TTC TAT AAC TCG GTC TTC ATG CAG AGA 2427
 197 Glu Tyr Asp Ser Ile Ile Val Phe Tyr Asn Ser Val Phe Met Gln Arg
 198 750 755 760
 199
 200 CTG AAA ACA AAT ATT TTG CAG TAT GCT TCC ACC AGG CCC CCT ACC TTG 2475
 201 Leu Lys Thr Asn Ile Leu Gln Tyr Ala Ser Thr Arg Pro Pro Thr Leu
 202 765 770 775
 203
 204 TCA CCA ATA CCT CAC ATT CCT CGA AGC CCT TAC AAG TTT CCT AGT TCA 2523
 205 Ser Pro Ile Pro His Ile Pro Arg Ser Pro Tyr Lys Phe Pro Ser Ser
 206 780 785 790 795
 207
 208 CCC TTA CGG ATT CCT GGA GGG AAC ATC TAT ATT TCA CCC CTG AAG AGT 2571
 209 Pro Leu Arg Ile Pro Gly Gly Asn Ile Tyr Ile Ser Pro Leu Lys Ser
 210 800 805 810
 211
 212 CCA TAT AAA ATT TCA GAA GGT CTG CCA ACA CCA ACA AAA ATG ACT CCA 2619
 213 Pro Tyr Lys Ile Ser Glu Gly Leu Pro Thr Pro Thr Lys Met Thr Pro
 214 815 820 825
 215

216	AGA TCA AGA ATC TTA GTA TCA ATT GGT GAA TCA TTC GGG ACT TCT GAG	2667
217	Arg Ser Arg Ile Leu Val Ser Ile Gly Glu Ser Phe Gly Thr Ser Glu	
218	830 835 840	
219		
220	AAG TTC CAG AAA ATA AAT CAG ATG GTA TGT AAC AGC GAC CGT GTG CTC	2715
221	Lys Phe Gln Lys Ile Asn Gln Met Val Cys Asn Ser Asp Arg Val Leu	
222	845 850 855	
223		
224	AAA AGA AGT GCT GAA GGA AGC AAC CCT CCT AAA CCA CTG AAA AAA CTA	2763
225	Lys Arg Ser Ala Glu Gly Ser Asn Pro Pro Lys Pro Leu Lys Lys Leu	
226	860 865 870 875	
227		
228	CGC TTT GAT ATT GAA GGA TCA GAT GAA GCA GAT GGA AGT AAA CAT CTC	2811
229	Arg Phe Asp Ile Glu Gly Ser Asp Glu Ala Asp Gly Ser Lys His Leu	
230	880 885 890	
231		
232	CCA GGA GAG TCC AAA TTT CAG CAG AAA CTG GCA GAA ATG ACT TCT ACT	2859
233	Pro Gly Glu Ser Lys Phe Gln Gln Lys Leu Ala Glu Met Thr Ser Thr	
234	895 900 905	
235		
236	CGA ACA CGA ATG CAA AAG CAG AAA ATG AAT GAT AGC ATG GAT ACC TCA	2907
237	Arg Thr Arg Met Gln Lys Gln Lys Met Asn Asp Ser Met Asp Thr Ser	
238	910 915 920	
239		
240	AAC AAG GAA GAG AAA TGAGGATCTC AGGACCTTGG TGGACACTGT GTACACCTCT	2962
241	Asn Lys Glu Glu Lys	
242	925	
243		
244	GGATTCTATTG TCTCTCACAG ATGTGACTGT AT	2994

1 36. A pharmaceutical composition of claim 32, wherein said RB cDNA
 2 fragment is selected from the group consisting of RB-1, RB-2, RB-5, γ 79R8 and mixtures
 3 thereof.

1 37. A pharmaceutical composition of claim 32, wherein a resulting mRNA
 2 transcript of said RB cDNA fragment has 4.6 kb.

1 38. A pharmaceutical composition of claim 37, wherein the cloned
 2 genomic DNA has at least 27 exons.

1 39. A pharmaceutical composition of claim 30, wherein the cloned RB
 2 cDNA transcribes into mRNA which translates in protein having an amino acid sequence
 3 comprising:

4	M P P K T P R K T A A T A A A A E P P A P P P P P P E E D P E	(3 4)
5	Q D S G P E D L P L V R L E F E E T E E P D F T A L C Q K L K I P D H V R E R A	(7 4)
6	W L T W E K V S S V D G V L G G Y I Q K K K E L W G I C I F I A A V D L D E M S	(1 1 4)
7	F T F T E L Q K N I E I S V H K F F N L L K E I D T S T K V D N A M S R L L K K	(1 5 4)
8	Y D V L F A L F S K L E R T C E L I Y L T Q P S S S I S T E I N S A L V L K V S	(1 9 4)
9	W I T F L L A K G E V L Q M E D D L V I S F Q L N L C V L D Y F I K L S P P M L	(2 3 4)
10	L K E P Y K T A V I P I N G S P R T P R R G Q M R S A R I A K Q L E N D T R I I	(2 7 4)
11	E V L C K E H E C N I D E V K N V Y F K N F I P F M N S L G L V T S N G L P E V	(3 1 4)
12	E N L S K R Y E E I Y L K N K D L D A R L F L D H D K T L Q T D S I D S F E T Q	(3 5 4)
13	R T P R K S N L D E E V N V I P P H T P V R T V M N T I Q Q L M M I L N S A S D	(3 9 4)
14	Q P S E N L I S Y F N N C T V N P K E S I L K R V K D I G Y I F K E K F A K A V	(4 3 4)
15	G Q G C V E I G S Q R Y K L G V R L Y Y R V M E S M L K S E E R L S I Q N F S	(4 7 4)
16	K L L N D N I F H M S L L A C A L E V V M A T Y S R S T S Q N L D S G T D L S F	(5 1 4)
17	P W I L N V L N L K A F D F Y K V I E S F I K A E G N L T R E M I K H L E R C E	(5 5 4)
18	H R I M E S L A W L S D S P L F D L I K Q S K D R E G P T D H L E S A C P L N L	(5 9 4)
19	P L Q N N H T A A D M Y L S P V R S P K K G S T T R V N S T A N A E T Q A T S	(6 3 4)
20	A F Q T Q K P L K S T S L S L F Y K K V Y R L A Y L R L N T L C E R L L S E H P	(6 7 4)
21	E L E H I I W T L F Q H T L Q N E Y E L M R D R H L D Q I M M C S M Y G I C K V	(7 1 4)
22	K N I D L K F K I I I V T A Y K D L P H A V Q E T F K R V L I K E E Y D S I I V	(7 5 4)
23	F Y N S V F M Q R L K T N I L Q Y A S T R P P T L S P I P H I P R S P Y K F P S	(7 9 4)
24	S P L R I P G G N I Y I S P L K S P Y K I S E G L P T P T K M T P R S R I L V S	(8 3 4)
25	I G E S F G T S E K F Q K I N Q M V C N S D R V L K R S A E G S N P P K P L K K	(8 7 4)
26	L R F D I E G S D E A D G S K H L P G E S K F Q Q K L A E M T S T R T R M Q K Q	(9 1 4)
27	K M N D S M D T S N K E E K	(9 2 8)

single-letter abbreviations for the amino acid residues are:
A, Ala; C, Cys; D, Asp; E, Gly; F, Phe; G, Gly; H, His;
I, Ile; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q, Gln;
R, Arg; S, Ser; T, Thr; V, Val; W, Trp; and Y, Tyr.

40. A DNA nucleotide sequence comprising:

```

2 TTCCGGTTTT TCTCAGGGGA CGTTGAAATT ATTTTGTA CGGGAGTCGG GAGAGGACGG 60
3
4
5 GGCGTGCCTT GCGTGCCTGGC GCGTCGTCCCT CCCCCGGCGCT CCTCCACAGC TCGCTGGCTC 120
6
7 CCGCCGCGGA AAGGCGTC ATG CCG CCC AAA ACC CCC CGA AAA ACG GCC GCC 171
8 Met Pro Pro Lys Thr Pro Arg Lys Thr Ala Ala
9 1 5 10
10
11 ACC GCC GCC GCT GCC GCG GAA CCC CCG GCA CCG CCG CCG CCG CCC 219
12 Thr Ala Ala Ala Ala Ala Glu Pro Pro Ala Pro Pro Pro Pro Pro
13 15 20 25
14
15 CCT CCG TAG GAG GAC CCA GAG CAG GAC AGC GGC CCG GAG GAC CTG CCT 267
16 Pro Pro Glu Glu Asp Pro Glu Gln Asp Ser Gly Pro Glu Asp Leu Pro
17 30 35 40
18
19 CTC GTC AGG CTT GAG TTT GAA GAA ACA GAA GAA CCT GAT TTT ACT GCA 315
20 Leu Val Arg Leu Glu Phe Glu Glu Thr Glu Glu Pro Asp Phe Thr Ala
21 45 50 55
22
23 TTA TGT CAG AAA TTA AAG ATA CCA GAT CAT GTC AGA GAG AGA GCT TGG 363

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24 Leu Cys Gln Lys Leu Lys Ile Pro Asp His Val Arg Glu Arg Ala Trp
 25 60 65 70 75
 26
 27 TTA ACT TGG GAG AAA GTT TCA TCT GTG GAT GGA GTA TTG GGA GGT TAT 411
 28 Leu Thr Trp Glu Lys Val Ser Ser Val Asp Gly Val Leu Gly Gly Tyr
 29 80 85 90
 30
 31 ATT CAA AAG AAA AAG GAA CTG TGG GGA ATC TGT ATC TTT ATT GCA GCA 459
 32 Ile Gln Lys Lys Glu Leu Trp Gly Ile Cys Ile Phe Ile Ala Ala
 33 95 100 105
 34
 35 GTT GAC CTA GAT GAG ATG TCG TTC ACT TTT ACT GAG CTA CAG AAA AAC 507
 36 Val Asp Leu Asp Glu Met Ser Phe Thr Phe Thr Glu Leu Gln Lys Asn
 37 110 115 120
 38
 39 ATA GAA ATC AGT GTC CAT AAA TTC TTT AAC TTA CTA AAA GAA ATT GAT 555
 40 Ile Glu Ile Ser Val His Lys Phe Phe Asn Leu Leu Lys Glu Ile Asp
 41 125 130 135
 42
 43 ACC AGT ACC AAA GTT GAT AAT GCT ATG TCA AGA CTG TTG AAG AAC TAT 603
 44 Thr Ser Thr Lys Val Asp Asn Ala Met Ser Arg Leu Leu Lys Lys Tyr
 45 140 145 150 155
 46
 47 GAT GTA TTG TTT GCA CTC TTC AGC AAA TTG GAA AGG ACA TGT GAA CTT 651
 48 Asp Val Leu Phe Ala Leu Phe Ser Lys Leu Glu Arg Thr Cys Glu Leu
 49 160 165 170
 50
 51 ATA TAT TTG ACA CAA CCC AGC AGT TCG ATA TCT ACT GAA ATA AAT TCT 699
 52 Ile Tyr Leu Thr Gln Pro Ser Ser Ser Ile Ser Thr Glu Ile Asn Ser
 53 175 180 185
 54
 55 GCA TTG GTG CTA AAA GTT TCT TGG ATC ACA TTT TTA TTA GCT AAA GGG 747
 56 Ala Leu Val Leu Lys Val Ser Trp Ile Thr Phe Leu Leu Ala Lys Gly
 57 190 195 200
 58
 59 GAA GTA TTA CAA ATG GAA GAT GAT CTG GTG ATT TCA TTT CAG TTA ATG 795
 60 Glu Val Leu Gln Met Glu Asp Asp Leu Val Ile Ser Phe Gln Leu Met
 61 205 210 215
 62 CTA TGT GTC CTT GAC TAT TTT ATT AAA CTC TCA CCT CCC ATG TTG CTC 843
 63 Leu Cys Val Leu Asp Tyr Phe Ile Lys Leu Ser Pro Pro Met Leu Leu
 64 220 225 230 235
 65
 66 AAA GAA CCA TAT AAA ACA GCT GTT ATA CCC ATT AAT GGT TCA CCT CGA 891
 67 Lys Glu Pro Tyr Lys Thr Ala Val Ile Pro Ile Asn Gly Ser Pro Arg
 68 240 245 250
 69
 70 ACA CCC AGG CGA GGT CAG AAC AGG AGT GCA CGG ATA GCA AAA CAA CTA 939
 71 Thr Pro Arg Arg Gly Gln Asn Arg Ser Ala Arg Ile Ala Lys Gln Leu
 72 255 260 265
 73
 74 GAA AAT GAT ACA AGA ATT ATT GAA GTT CTC TGT AAA GAA CAT GAA TGT 987
 75 Glu Asn Asp Thr Arg Ile Ile Glu Val Leu Cys Lys Glu His Glu Cys
 76 270 275 280
 77
 78 AAT ATA GAT GAG GTG AAA AAT GTT TAT TTC AAA AAT TTT ATA CCT TTT 1035
 79 Asn Ile Asp Glu Val Lys Asn Val Tyr Phe Lys Asn Phe Ile Pro Phe
 80 285 290 295
 81
 82 ATG AAT TCT CTT GGA CTT GTA ACA TCT AAT GGA CTT CCA GAG GTT GAA 1083
 83 Met Asn Ser Leu Gly Leu Val Thr Ser Asn Gly Leu Pro Glu Val Glu
 84 300 305 310 315

146	CGA ATC ATG GAA TCC CTT GCA TGG CTC TCA GAT TCA CCT TTA TTT GAT	1851
147	Arg Ile Met Glu Ser Leu Ala Trp Leu Ser Asp Ser Pro Leu Phe Asp	
148	560 565 570	
149		
150	CTT ATT AAA CAA TCA AAG GAC CGA GAA GGA CCA ACT GAT CAC CTT GAA	1899
151	Leu Ile Lys Gln Ser Lys Asp Arg Glu Gly Pro Thr Asp His Leu Glu	
152	575 580 585	
153		
154	TCT GCT TGT CCT CTT AAT CTT CCT CTC CAG AAT AAC CAC ACT GCA GCA	1947
155	Ser Ala Cys Pro Leu Asn Leu Pro Leu Gln Asn Asn His Thr Ala Ala	
156	590 595 600	
157		
158	GAT ATG TAT CTT TCT CCT GTA AGA TCT CCA AAG AAA AAA GGT TCA ACT	1995
159	Asp Met Tyr Leu Ser Pro Val Arg Ser Pro Lys Lys Lys Gly Ser Thr	
160	605 610 615	
161		
162	ACG CGT GTA AAT TCT ACT GCA AAT GCA GAG ACA CAA GCA ACC TCA GCC	2043
163	Thr Arg Val Asn Ser Thr Ala Asn Ala Glu Thr Gln Ala Thr Ser Ala	
164	620 625 630 635	
165		
166	TTC CAG ACC CAG AAG CCA TTG AAA TCT ACC TCT CTT TCA CTG TTT TAT	2091
167	Phe Gln Thr Gln Lys Pro Leu Lys Ser Thr Ser Leu Ser Leu Phe Tyr	
168	640 645 650	
169		
170	AAA AAA GTG TAT CGG CTA GCC TAT CTC CGG CTA AAT ACA CTT TGT GAA	2139
171	Lys Lys Val Tyr Arg Leu Ala Tyr Leu Arg Leu Asn Thr Leu Cys Glu	
172	655 660 665	
173		
174	CGC CTT CTG TCT GAG CAC CCA GAA TTA GAA CAT ATC ATC TGG ACC CTT	2187
175	Arg Leu Leu Ser Glu His Pro Glu Leu Glu His Ile Ile Trp Thr Leu	
176	670 675 680	
177		
178	TTC CAG CAC ACC CTG CAG AAT GAG TAT GAA CTC ATG AGA GAC AGG CAT	2235
179	Phe Gln His Thr Leu Gln Asn Glu Tyr Glu Leu Met Arg Asp Arg His	
180	685 690 695	
181		
182	TTG GAC CAA ATT ATG ATG TGT TCC ATG TAT GGC ATA TGC AAA GTG AAG	2283
183	Leu Asp Gln Ile Met Met Cys Ser Met Tyr Gly Ile Cys Lys Val Lys	
184	700 705 710 715	
185		
186	AAT ATA GAC CTT AAA TTC AAA ATC ATT GTA ACA GCA TAC AAG GAT CTT	2331
187	Asn Ile Asp Leu Lys Phe Lys Ile Ile Val Thr Ala Tyr Lys Asp Leu	
188	720 725 730	
189		
190	CCT CAT GCT GTT CAG GAG ACA TTC AAA CGT GTT TTG ATC AAA GAA GAG	2379
191	Pro His Ala Val Gln Glu Thr Phe Lys Arg Val Leu Ile Lys Glu Glu	
192	735 740 745	
193		
194	GAG TAT GAT TCT ATT ATA GTA TTC TAT AAC TCG GTC TTC ATG CAG AGA	2427
195	Glu Tyr Asp Ser Ile Ile Val Phe Tyr Asn Ser Val Phe Met Gln Arg	
196	750 755 760	
197		
198	CTG AAA ACA AAT ATT TTG CAG TAT GCT TCC ACC AGG CCC CCT ACC TTG	2475
199	Leu Lys Thr Asn Ile Leu Gln Tyr Ala Ser Thr Arg Pro Pro Thr Leu	
200	765 770 775	
201		
202	TCA CCA ATA CCT CAC ATT CCT CGA AGC CCT TAC AAG TTT CCT AGT TCA	2523
203	Ser Pro Ile Pro His Ile Pro Arg Ser Pro Tyr Lys Phe Pro Ser Ser	
204	780 785 790 795	
205		
206	CCC TTA CGG ATT CCT GGA GGG AAC ATC TAT ATT TCA CCC CTG AAG AGT	2571

207	Pro Leu Arg Ile Pro Gly Gly Asn Ile Tyr Ile Ser Pro Leu Lys Ser			
208	800	805	810	
209				
210	CCA TAT AAA ATT TCA GAA GGT CTG CCA ACA CCA ACA AAA ATG ACT CCA		2619	
211	Pro Tyr Lys Ile Ser Glu Gly Leu Pro Thr Pro Thr Lys Met Thr Pro			
212	815	820	825	
213				
214	AGA TCA AGA ATC TTA GTA TCA ATT GGT GAA TCA TTC GGG ACT TCT GAG		2667	
215	Arg Ser Arg Ile Leu Val Ser Ile Gly Glu Ser Phe Gly Thr Ser Glu			
216	830	835	840	
217				
218	AAG TTC CAG AAA ATA AAT CAG ATG GTA TGT AAC AGC GAC CGT GTG CTC		2715	
219	Lys Phe Gln Lys Ile Asn Gln Met Val Cys Asn Ser Asp Arg Val Leu			
220	845	850	855	
221				
222	AAA AGA AGT GCT GAA GGA AGC AAC CCT CCT AAA CCA CTG AAA AAA CTA		2763	
223	Lys Arg Ser Ala Glu Gly Ser Asn Pro Pro Lys Pro Leu Lys Lys Leu			
224	860	865	870	875
225				
226	CGC TTT GAT ATT GAA GGA TCA GAT GAA GCA GAT GGA AGT AAA CAT CTC		2811	
227	Arg Phe Asp Ile Glu Gly Ser Asp Glu Ala Asp Gly Ser Lys His Leu			
228	880	885	890	
229				
230	CCA GGA GAG TCC AAA TTT CAG CAG AAA CTG GCA GAA ATG ACT TCT ACT		2859	
231	Pro Gly Glu Ser Lys Phe Gln Gln Lys Leu Ala Glu Met Thr Ser Thr			
232	895	900	905	
233				
234	CGA ACA CGA ATG CAA AAG CAG AAA ATG AAT GAT AGC ATG GAT ACC TCA		2907	
235	Arg Thr Arg Met Gln Lys Gln Lys Met Asn Asp Ser Met Asp Thr Ser			
236	910	915	920	
237				
238	AAC AAG GAA GAG AAA TGAGGATCTC AGGACCTTGG TGGACACTGT GTACACCTCT		2962	
239	Asn Lys Glu Glu Lys			
240	925			
241				
242	GGATTTCATTG TCTCTCACAG ATGTGACTGT AT		2994	

1 41. A method of therapeutically treating inactive, mutative or absent
 2 cancer suppressing genes comprising:
 3 treating said inactive, mutative or absent cancer suppressing genes with at
 4 least a portion of intact cancer suppressing genes.

1 42. A method of claim 41, wherein said cancer suppressing genes are each
 2 a substance selected from the groups consisting of RB genes, breast cancer suppressing
 3 genes, Wilm's tumor suppressing genes, Beckwith-Wiedemann syndrome suppressing genes,
 4 bladder transitional cell carcinoma suppressing genes, neuroblastoma suppressing genes,
 5 small cell lung carcinoma suppressing genes, renal cell carcinoma suppressing genes,
 6 acoustic neuroma suppressing genes, colorectal carcinoma suppressing genes, and mixtures
 7 thereof.

1 43. A method of claim 41, wherein said treating includes:

2 treating said inactive, mutative or absent cancer suppressing gene with a
3 substance selected from the group consisting of an RB gene, a portion of said gene, or a
4 mixture thereof.

1 44. A method of claim 43, wherein said portion is selected from the group
2 consisting of RB cDNA, RB cDNA fragment, homologues thereof and mixtures thereof.

1 45. The method of claim 41, wherein the intact cancer suppressing gene, or a
2 portion thereof, is delivered to the site of a tumor by means of a retrovirus.

1 46. A method of claim 41, wherein the intact cancer suppressing gene, or a
2 portion thereof, is delivered to the site of a tumor by a liposome.

1 47. A method of claim 41, wherein the location of said cancer suppressing
2 gene is determined by utilizing a genetic marker.